Infections de prothèse ostéo-articulaire traitées par débridement : facteurs prédictifs d'échec [Predictors of failure for prosthetic joint infections treated with debridement]

B. Letouvet, C. Arvieux, H. Leroy, J.-L. Polard, J.-M. Chapplain, H. Common, C. Ecoffey, D. Huten, A. Jolivet-Gougeon, P. Tattevin

Facteurs prédictifs d'échec pour les infections de prothèse ostéo-articulaire traitées par lavage articulaire

Predictors of failure for prosthetic joint infections treated with debridement

B. Letouvet,[a] C. Arvieux,[b,c] H. Leroy,[b,c] J-L. Polard,[c,d] J-M. Chapplain,[b,c] H. Common,[c,d] C. Ecoffey,[a] D. Huten,[c,d] A. Jolivet-Gougeon,[c,e] P. Tattevin,[b,c] *

[a]Réanimation Chirurgicale et Anesthésie, Hôpital Pontchaillou, rue Le Guilloux, Université Rennes-1, 35033 Rennes, France

[b]Maladies Infectieuses et Réanimation Médicale, Hôpital Pontchaillou, rue Le Guilloux, Université Rennes-1, 35033 Rennes, France

[c]Centre de Référence des Infections Ostéo-Articulaires Complexes (CRIOAC), Hôpital Pontchaillou, rue Le Guilloux, Université Rennes-1, 35033 Rennes, France

[d]Orthopédie-Traumatologie, Hôpital Pontchaillou, rue Le Guilloux, Université Rennes-1, 35033 Rennes, France

[e]Département de Bactériologie et d'Hygiène Hospitalière, Hôpital Pontchaillou, rue Le Guilloux, Université Rennes-1, 35033 Rennes, France

*** Auteur correspondant :** Service des Maladies Infectieuses et Réanimation Médicale, CHU Pontchaillou, 35033 Rennes cedex, France. e-mail: pierre.tattevin@chu-rennes.fr

Contributions of authors: BL, CA and PT planned the study design; BL, HL, and JMC performed the statistical analysis; BL and PT wrote the first draft; BL, CA, HL, JLP, JMC, HC, CE, DH, AJG, and PT were involved in the management of patients enrolled in the study, contributed to the manuscript, and reviewed the final version before submission.

Abstract

Objectifs: Certaines infections de prothèse ostéo-articulaire (IPO) guérissent après un lavage articulaire avec conservation de la prothèse. Pour mieux préciser les patients candidats à cette chirurgie conservatrice, nous souhaitions identifier les facteurs indépendamment associés à son succès.

Méthodes: Etude observationnelle des IPO initialement traitées par lavage dans notre institution entre 2008 et 2011, avec >6 mois de suivi post-traitement.

Résultats: Soixante patients consécutifs avec IPO (hanche, n=34; genou, n=26), ont été inclus. Les échecs (n=20, 33%), prédéfinis par la persistance de signes d'IPO ou la rechute, ont nécessité une chirurgie complémentaire (n=17), et/ou une antibiothérapie suppressive (n=6). Les facteurs indépendamment associés à l'échec étaient une chirurgie antérieure sur la prothèse (odds ratio 6.3[1.8-22.3]), une IPO à *Staphylococcus aureus* (OR 9.4[1.6-53.9]) et une durée d'antibiothérapie post-lavage <3 mois (OR 20.0[2.2-200]).

Conclusions: Une chirurgie antérieure, une IPO à *S. aureus* et une antibiothérapie brève sont associées au risque d'échec après lavage.

*Mots clés***:** Infection de prothèse ostéo-articulaire; *Staphylococcus aureus*; lavage

Abstract

Objectives: Prosthetic joint infections (PJI) may be cured in selected patients with a surgical strategy based on debridement and prosthesis retention. To better target patients most likely to benefit from this conservative strategy, we aimed to identify factors predictive for success.

Methods: We performed an observational study of PJI initially treated with debridement during years 2008-2011 in our institution, and >6 months post-treatment follow-up.

Results: Sixty consecutive patients with PJI (hip, n=34; knee, n=26), fulfilled inclusion criteria. Failures (n=20, 33%), predefined as persistence of PJI signs or relapses, were managed with additional surgery (n=17), and/or lifelong suppressive antimicrobial agents (n=6). Variables independently associated with failure were previous surgery on the prosthetic joint (odds ratio 6.3[1.8-22.3]), *Staphylococcus aureus* PJI (OR 9.4[1.6-53.9]), and antibacterial treatment duration post-debridement <3 months (OR 20.0[2.2-200]).

Conclusions: Previous surgery, *S. aureus* PJI, and short antibacterial treatment, are associated with increased risk of failure after debridement.

*Key words***:** Prosthetic joint infections; *Staphylococcus aureus*; debridement

1. Introduction

The burden of prosthetic joint infections (PJI) is increasing in developed countries, due to increasing number of patients who underwent arthroplasty [1]. A recent literature review estimated that 0.9% (95% confidence interval, 0.4%-2.2%) of primary total hip arthroplasty will become infected [2]. Despite growing interest in the field, treatment of PJI remains poorly standardized. A significant proportion of patients are initially managed with debridement and prosthesis retention, associated with prolonged antibacterial treatment. This conservative strategy has the theoretical advantage of simplifying the surgical procedure(s), and may allow earlier recovery of functional joint, but success rates are sub-optimal [3-6]. To better target the patients who are most likely to benefit from this conservative strategy, we aimed to identify factors predictive for success.

2. Methods

The study was performed in a 1,600-bed tertiary care center, which serves as a referral for the management of complicated osteo-articular infections in the area (population catchment, one million inhabitants). PJI are discussed during weekly multidisciplinary meetings with a panel of specialists in orthopedic surgery, infectious diseases, microbiology, and radiology, in line with national and international guidelines [7,8]. Antibacterial treatment is initiated per-operatively, after 5 samples of infected tissues have been collected, with a combination of vancomycin/gentamicin/piperacillin-tazobactam when no indication on the pathogen(s) involved is available, or vancomycin/gentamicin for Gram positive cocci, or piperacillin-tazobactam for Gram negative bacilli, or a regimen based on the pathogen(s) susceptibility testing, if available (i.e., when microbiological documentation have been obtained pre-operatively through blood cultures and/or joint aspirates).

We performed an observational study of all patients with PJI initially treated with debridement and prosthesis retention. Cases were identified through a computerized database, and data were extracted from medical charts and surgery reports, through a standardized questionnaire. Data collected included demographics, comorbidities, PJI diagnosis and management, with a special focus on surgical technique, antibacterial treatment, and follow-up. PJI was defined by presence of pus in the joint, and/or the growth of a virulent microorganism (e.g. *Staphylococcus aureus*, Gram-negative bacilli) in a specimen of periprosthetic tissue, or synovial fluid. For organism considered as possible contaminant (coagulase-negative staphylococci, *Propionibacterium acnes*), at least two positive cultures were required [7,8]. Outcome was classified as failure in case of: i) persistence of PJI signs during treatment, or relapses after treatment discontinuation, with ≥ 1 pathogen isolated from osteo-articular samples, and/or ii) additional surgery required for sepsis control. Request for informed consent was waived by our institutional review board, as the study was retrospective, observational, and collected data anonymously.

Quantitative variables were presented as mean ± standard deviation. Qualitative variables were expressed as percentages. Cases classified as failures were compared to cases who did not meet criteria for failure during at least 6 months after antibacterial treatment was discontinued, using Wilcoxon tests for quantitative variables, and Chi^2 tests for qualitative variables. To identify variables independently predictive of failure, we included all variables with $P<0.10$ in the bivariate analysis, in a multivariate logistic regression analysis step-by-step. Statistical analysis was done with SAS 9.2 (SAS Institute, Cary, NC, USA). $P<0.05$ was considered statistically significant.

3. Results

3.1 Patients characteristics

Sixty consecutive patients with PJI (34 men, 26 women), were initially managed with prosthesis retention and debridement in our institution during years 2008-2011 (Table I). Of note, no striking discrepancy with guidelines was identified during medical charts review: all patients could be candidates for debridement, according to published criteria (i.e. PJI with well-fixed prosthesis, without sinus tract, within 30 days of prosthetic implantation, or < 3 weeks from symptoms onset [7,8]). PJI was microbiologically documented in 54 patients, including one polymicrobial (meticillin-susceptible *S. aureus* and *Proteus mirabilis*), 44 Gram positive, and nine Gram negative PJI. Most common pathogens were *S. aureus* (n=24, including 6 meticillin-resistant), coagulase-negative staphylococci (n=8, including 6 meticillin-resistant), and Enterobacteriaceae. Resistance to rifampin was found in two coagulase-negative staphylococci (25%), and in no *S. aureus*. Resistance to fluoroquinolones was found in six *S. aureus* (25%), in four coagulase-negative staphylococci (50%), and in no Enterobacteriaceae. Rifampin was prescribed in 34 patients, and fluoroquinolones in 30 patients.

3.2 Outcome

Twenty patients (33%) presented at least one criteria for failure and were managed with additional surgical treatment (n=17), including repeated debridement (n=6), one-stage prosthesis exchange (n=5), two-stage prosthesis exchange (n=8), and/or life-long suppressive antibacterial treatment (n=6). Of note, patients could combine multiple criteria for failure (e.g., need for repeated debridement, then prosthesis exchange or lifelong suppressive antibacterial treatment). Median delay between antibacterial treatment discontinuation and diagnosis of failure was 30 days.

3.3 Risk factors for treatment failure

Variables significantly associated with failure on univariate analysis (Table II) were previous surgery on the prosthetic joint (mean number, 0.95 ± 0.18 vs. 0.48 ± 0.12, *P*=0.03), *S. aureus* PJI (60% vs. 30%, *P*=0.025), and duration of antimicrobial treatment (mean, 57 ± 32 days vs. 101 ± 55, *P*=0.015). On multivariate analysis, previous surgery (odds ratio 6.3, CI95% [1.8-22.3]), *S. aureus* PJI (OR 9.4 [1.6-53.9]), and antibacterial treatment duration post-debridement <3 months (OR 20.0[2.2-200]) were independently associated with increased risk of failure.

4. Discussion

Initial management of PJI with debridement and prosthesis retention is a seducing alternative to prosthesis replacement, and has been associated with increasing rates of success, from 21-28% before 2000 [3-4], to 75-78% in more recent series [5-6]. However, when this conservative strategy is applied to PJI unlikely to be cured without prosthesis removal, their appropriate surgical management is delayed, which may lead to iterative surgeries, prolonged antibacterial treatment, and poor functional outcome [9-14]. Hence, debridement should be limited to patients likely to benefit from this strategy: PJI with well-fixed prosthesis, without sinus tract, within 30 days of prosthetic implantation, or < 3 weeks from symptoms onset [7,8].

In this observational study, although PJI were managed by a multidisciplinary team, with a strict adherence to guidelines, one third of those initially managed with debridement and prosthesis retention were classified as failure, with a median follow-up of 19 months after antibacterial treatment discontinuation. Two variables independently predictive of failure have already been identified by others: *S. aureus* PJI, and multiple previous surgeries, reduce the probability of success after debridement with prosthesis retention [7,8]. We aimed to identify modifiable factors associated with improved outcome: first, we found a trend toward better prognosis when debridement was performed through arthrectomy associated with polyethylene replacement (Table 2, P=0.08), as recommended [7,8,11,15]. Second, antibacterial regimen duration <3 months post-debridement was independently associated with failure. This suggests that PJI managed with debridement and prosthesis retention should be treated longer than PJI managed with prosthesis replacement, which makes sense, given that the quality of source control is probably lower when prosthesis is retained. Hence, the remaining inoculum would be higher, and would require longer duration of antimicrobial agents.

This study has limitations: i) as it was monocentric, its findings do not necessarily apply to other settings; ii) due to limited sample size, we may have missed factors associated with treatment outcome; iii) the observational design implies that confusion bias may occur, although the prognostic factors we identified remained significant on multivariate analysis; iv) although the median duration of follow-up was 19 months after antibacterial discontinuation (interquartile range, 12-27), late relapses may have been missed. Obviuosly, randomized controlled trials will collect more robust data on optimal antibacterial treatment duration: For example, the French DATIPO trial, that has just been recently completed, should bring ‘evidence-based’ data in this area, as patients with PJI could be enrolled whether their surgical treatment consisted of prosthesis replacement, or prosthesis retention with debridement.

However, all patients enrolled in the study presented herein were managed by a multidisciplinary team, following international guidelines, and probably reflect current management of PJI in many settings. In conclusion, this study suggests that patients with PJI initially managed with debridement and prosthesis retention are more likely to be cured with no need for additional surgical interventions if PJI occurred in the absence of multiple previous surgeries, when *S. aureus* is not involved, and if they receive prolonged antibacterial treatment after debridement.

Conflict of interest No competing interest declared

Acknowledgement The study was presented in part at the 23rdEuropean Congress of Clinical Microbiology and Infectious Diseases, April 2013, Berlin, Germany.

Table 1. Caractéristiques des patients

Table 1. Patients characteristics

Characteristics	Number (%) or median [interquartile range]
Age (years)	75 [66-82]
Prosthetic joint involved	hip, 34 (57%); knee, 26 (43%)
Comorbidities	
ASA score > 2	20 (33%)
Cardiac failure	15 (25%)
Diabetes	7 (12%)
Diagnosis of prosthetic joint infection	
Time from last surgery to symptoms onset (months)	2.6 [0.5-44]
Time from symptoms onset to debridement (days)	6 [4-11.5]
Fever > 38°C	39 (65%)
Erythema surrounding the joint area	33 (55%)
Purulent discharge	24 (40%)
White blood cells count before debridement (G/mm3)	10 [7-14]
C reactive protein before debridement (mg/L)	142 [76-250]
Positive blood culture(s)	19 (32%)
Debridement	
Duration (minutes)	80 [60-96]
Arthrectomy and polyethylene replacement not performed	21 (35%)
Microbiology	
Meticillin-susceptible *Staphylococcus aureus*	18 (30%)
Meticillin-resistant *S. aureus*	6 (10%)
Coagulase-negative staphylococci	8 (13%)
Streptococcus agalactiae	5 (8%)
Streptococcus equisimilis	2 (3%)
Escherichia coli	5 (8%)
Pseudomonas aeruginosa	3 (5%)
Others [a]	8 (13%)
Antibacterial treatment duration (days)	92 [76-108]
Follow-up after antibacterials discontinuation (months)[b]	19 [12-27]

ASA, American Society of Anesthesiology [a] *Proteus mirabilis, Klebsiella pneumoniae, Enterococcus faecalis, Streptococcus mitis, Streptococcus oralis, Finegoldia magna, Propionibacterium acnes, Peptostreptococcus* sp. [b] Range, 6-36

Table 2. Analyse univariée et multivariée des facteurs associés à l'échec du traitement

Table 2. Bivariate and multivariate analysis of factors associated with treatment failure

Variables	No failure (n=40)	Failure (n=20)	Univariate analysis *P*	Multivariate analysis Odds ratio	Multivariate analysis CI 95%
Age, years	73.3 ± 12.3	71.7 ± 12.4	0.65		
Diabetes, n (%)	4 (10)	3 (15)	0.53		
ASA score > 2, n (%)	12 (30)	8 (40)	0.44		
Hip prosthesis, n (%)	24 (60)	10 (50)	0.46		
Previous surgery, number	0.48 ± 0.12	0.95 ± 0.18	0.03	6.3	[1.8-22.3]
Time from last surgery to symptoms onset, months	4.6 ± 11	4.4 ± 7.3	0.9		
Time from symptoms onset to debridement, days	12.8 ± 16.8	7.5 ± 6.4	0.19		
CRP before surgery, mg/dL	155.7 ± 129.2	214.7 ± 95.4	0.13		
Positive blood cultures	11 (29)	8 (47)	0.19		
CRP > 220 mg/dL, n (%)	11 (28)	8 (57)	0.053		
Debridement without arthrectomy or polyethylene replacement, n (%)	11 (27.5)	10 (50)	0.085		
Debridement duration, hours	81.9 ± 31.4	94 ± 57.2	0.39		
Staphylococcus aureus PJI, n (%)	12 (30)	12 (60)	0.025	9.4	[1.6-53.9]
Antibacterial treatment duration, days	101.3 ± 55.3	57 ± 32.3	0.015		
Antibacterial treatment < 3 months *	14 (38)	12 (75)	0.013	20.0	[2.2-200]

* Failures diagnosed while the patient was still on antibacterial treatment were excluded to avoid survivor selection bias

Continuous variables are presented as mean ± standard deviation

ASA, American Society of Anesthesiology; PJI, Prosthetic Joint Infection; CI 95%, Confidence Interval 95%

References

[1] Del Pozo JL, Patel R. Clinical practice. Infection associated with prostheticjoints. N Engl J Med 2009;361(8):787–94.

[2] Lindeque B, Hartman Z, Noschenko A, Cruse M. Infection after primarytotal hip arthroplasty. Orthopedics 2014;37(4):257–65.

[3] Schoifet SD, Morrey BF. Treatment of infection after total knee arthroplastyby debridement with retention of the components. J Bone Joint Surg Am1990;72(9):1383–90.

[4] Tattevin P, Crémieux AC, Pottier P, Huten D, Carbon C. Prosthetic jointinfection: when can prosthesis salvage be considered? Clin Infect Dis1999;29(2):292–5.

[5] Senneville E, Joulie D, Legout L, Valette M, Dezèque H, Beltrand E,et al. Outcome and predictors of treatment failure in total hip/kneeprosthetic joint infections due to *Staphylococcus aureus*. Clin Infect Dis2011;53(4):334–40

.[6] Vilchez F, Martínez-Pastor JC, García-Ramiro S, Bori G, Maculé F, SierraJ, et al. Outcome and predictors of treatment failure in early post-surgicalprosthetic joint infections due to *Staphylococcus aureus* treated withdebridement. Clin Microbiol Infect 2011;17(3):439–44.

[7] Société de pathologie infectieuse de langue franc¸aise. Recommendationsfor bone and joint prosthetic device infections in clinical practice (prosthe-sis, implants, osteosynthesis). Med Mal Infect 2010;40(4):185–211.

[8] Osmon DR, Berbari EF, Berendt AR, et al. Executive summary: diagnosisand management of prosthetic joint infection: clinical practice guide-lines by the Infectious Diseases Society of America. Clin Infect Dis2013;56(1):1–10

.[9] Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. N EnglJ Med 2004;351(16):1645–54.

[10] Moran E, Masters S, Berendt AR, McLardy-Smith P, Byren I, Atkins BL.Guiding empirical antibiotic therapy in orthopaedics: the microbiology ofprosthetic joint infection managed by debridement, irrigation and prosthesisretention. J Infect 2007;55(1):1–7.

[11] Barberán J. Management of infections of osteoarticular prosthesis. ClinMicrobiol Infect 2006;12(3):93–101.

[12] Buller LT, Sabry FY, Easton RW, Klika AK, Barsoum WK. The preoperativeprediction of success following irrigation and debridement with polyeth-ylene exchange for hip and knee prosthetic joint infections. J Arthroplasty2012;27(6) [857-864.e1-4].

[13] Rodríguez D, Pigrau C, Euba G, Cobo J, García-Lechuz J, PalominoJ, et al. Acute haematogenous prosthetic joint infection: prospectiveevaluation of medical and surgical management. Clin Microbiol Infect2010;16(12):1789–95.

[14] Segawa H, Tsukayama DT, Kyle RF, Becker DA, Gustilo RB. Infectionafter total knee arthroplasty. A retrospective study of the treat-ment of eighty-one infections. J Bone Joint Surg Am 1999;81(10):1434–45.

[15] Marculescu CE, Berbari EF, Hanssen AD, Steckelberg JM, Harm-sen SW, Mandrekar JN, et al. Outcome of prosthetic joint infectionstreated with debridement and retention of components. Clin Infect Dis2006;42(4):471–8.